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Bleeding After Liver Biopsy

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During nine years 3,080 liver biopsies were carried out and bleeding occurred in 22 of the patients (0.7 percent). Transfusions were given to 17 of these patients and laparotomies were done to control the bleeding in six. All survived. Bleeding was evident within three hours in 19 patients, but occurred from 3 to 13 days after biopsy in the remaining three. Pain requiring analgesic medication and a fall in blood pressure were the usual indications that major bleeding had occurred. Relative contraindications to biopsy (particularly a prolonged prothrombin time) were present in 10 of the 22 bleeding patients and in only 2 of the 41 nonbleeding controls ($P<0.001$). We believe that some of the bleeding episodes could have been prevented with more careful attention to the indications and contraindications to biopsy, and more rigorous correction of recognized clotting abnormalities.

PERCUTANEOUS LIVER BIOPSY is used widely for the diagnosis, staging and follow-up of hepatic disease. Complications of this procedure include pain, bleeding, pneumothorax, bile peritonitis, arteriovenous fistula formation, intrahepatic hematomas, bacteremia and inadvertently taking specimens from other organs.[1-7] Of the serious complications, bleeding is the most common, with an incidence ranging from 0.8 percent to 1 percent.[1,5,6] Subsequent fatality may occur in as many as 3 out of 10,000 biopsies.[6]

In this report, we describe our experience with postbiopsy bleeding in 22 patients and provide a partial explanation for its occurrence.

Patients and Methods

A total of 3,080 percutaneous liver biopsies were carried out in adult patients at the Stanford University Medical Center, the Santa Clara Valley Medical Center and the Veterans Administration Medical Center from January 1970 through December 1978. In all patients, evaluations were done by the gastroenterology consultation team or their private physicians before biopsy. Most biopsies were done either by the medical resident or gastroenterology fellow; 18 percent were done by physicians in private practice.

The biopsies were done by the suction aspiration technique using a modified Menghini (Klatskin) needle.[8] The approach was transthoracic with the patient lying on his back and holding his breath. The point of entry was between the midaxillary and posterior axillary line. After biopsy the patient was advised to lie on his right side for two hours and remain in bed overnight. A total of 171 patients who had liver biopsies done as outpatients were allowed to leave six hours after the procedures and advised to rest at home.

Contraindications to liver biopsy during the study period were a prothrombin time less than 50 percent, partial thromboplastin time greater

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than 10 seconds over control, a platelet count less than 50,000 or an abnormal bleeding time.

There were 22 patients who bled following liver biopsy (suspected on clinical grounds and confirmed by a drop in hematocrit of 5 hematocrit points or greater). The charts of these patients were reviewed in detail. For purposes of comparison we randomly selected the cases of 44 patients from the remaining 3,036 patients. The charts of 41 were available for review.

The data were analyzed by the two sample Student T test for continuous data or by the chi-square test for categorical data. Yates' correction for continuity was used in calculating the chi-square statistic when the expected frequencies were less than 5.[9]

TABLE 1.—*Age, Sex, Hematocrit, Indications for Biopsy and Histologic Diagnoses*

	Bleeding Group (22)	*Control Group (41)*
Age	46±3	46±2
Sex (male/female)	14/8	23/18
Hematocrit (percent)	34±2	37±1
Indications for biopsy		
Alcoholic liver disease	5	11
Acute hepatitis	6	5
Chronic hepatitis	3	2
Other*	8	23
Histologic diagnoses		
Acute viral hepatitis	2	2
Chronic persistent hepatitis	2	2
Chronic active hepatitis	2	2
Cirrhosis and chronic active hepatitis	0	1
Alcoholic hepatitis	5	2
Alcoholic cirrhosis	0	6
Alcoholic cirrhosis and hepatoma	1	0
Metastatic cancer	0	3
Lymphoma	1	2
Granulomatous hepatitis	3	0
Cholestatic hepatitis	1	3
Minor abnormalities (triaditis, congestion, fat, extramedullary hematopoiesis)†	2	13
Normal†	2	5
No liver tissue	1	0

*Includes biopsy for abnormal liver function tests, hepatomegaly, lymphoma staging, possible methotrexate toxicity and so forth.

†The observed difference between bleeding and control groups for those with minor abnormalities or a normal liver is significant at $P<0.05$.

TABLE 2.—*Treatment for Bleeding After Biopsy*

	Number of Patients	*Units of Blood**
Intravenous fluids	5	0
Transfusions	11	3±0.3
Transfusions and laparotomy	6	12±3

*Given as mean±1 S.E.M.

Results

Incidence of Bleeding, Patient Characteristics, Treatment and Outcome

In all, 3,080 percutaneous liver biopsies were carried out at our three hospitals during nine years. Twenty-two patients (0.7 percent) bled following biopsy. Table 1 gives the age, sex, prebiopsy hematocrit, indications for biopsy, and histologic diagnoses in the bleeding patients and the control group. Bleeding patients were less likely than those in the control group to have normal liver tissue or minor histologic abnormalities ($P<0.05$). In other respects, the groups were comparable.

Treatment given to the 22 patients who bled is shown in Table 2. The five patients in whom no transfusions were needed had a mean hematocrit drop of 9 hematocrit points. In 11 patients transfusions were required to maintain vital signs, but their bleeding stopped spontaneously. In one patient in this group it was necessary to place a chest tube to drain a bloody right pleural effusion. Six patients continued to bleed and went to laparotomy after receiving an average of 12 units of blood (range 5 to 21 units). The findings were a hepatic artery to gall bladder fistula in one patient, a pinpoint puncture wound in two patients and lacerations of the right lobe of the liver in three patients. Five patients had at least 1,500 ml of blood in the peritoneal cavity and three had large intrahepatic hematomas that required draining. Surgical operations were not always simple, requiring two or more hours in four patients. Postoperative recovery was uneventful. All patients survived and were later discharged from hospital.

Initial Indications of Bleeding

Changes in vital signs and right upper quadrant pain requiring analgesia were the usual indications that a major hemorrhage had occurred (Table 3). The most common finding was a simultaneous drop in blood pressure and rise in pulse rate. In seven patients hypotension developed without a compensatory rise in pulse. Tachycardia without hypertension developed in one patient in both the bleeding and control groups. Vital sign changes were apparent within three hours in 19 patients who bled soon after biopsy. One of these patients stopped bleeding within 24 hours only to bleed again four days later. Three patients had stable hematocrits following biopsy, but then bled from 3 to 13 days later. Two of these three patients had

significant right upper quadrant pain immediately after the biopsy, but it subsided within six hours. Two of the four patients with delayed episodes of bleeding had hematobilia.

Pain requiring analgesia was noted immediately following biopsy in 12 bleeding patients and in only 5 control patients ($P<0.001$). All 12 patients had pain in the right upper quadrant or epigastrium. Four had pain in the right shoulder and three had pleuritic pain as well.

Examination at the time of bleeding found moderate to pronounced right upper quadrant tenderness in 17 of the 22 patients. Rebound tenderness was found in seven patients, and in six of these laparotomy was eventually required.

Etiologic Factors

Relative contraindications to liver biopsy are shown in Table 4. Ten patients in the bleeding group (45 percent) had one or more relative contraindications to liver biopsy whereas only two patients in the control group (5 percent) had any such abnormalities ($P<0.001$). In the bleeding group, seven patients had a single contraindication to biopsy and three had several. The prothrombin time identified six of these patients and was the only discriminating test ($P<0.003$).

The responsible physician chose to do the biopsy despite the contraindications to the procedure for varying reasons. In three patients the prothrombin time was in the 40 percent to 50 percent range. It was believed that the benefits of obtaining the histologic diagnosis outweighed the potential risk with this modest reduction in prothrombin time. Fresh frozen plasma was given to three other patients whose prothrombin times ranged from 30 percent to 40 percent. It rose to 59 percent in one patient, but no follow-up was done in the other two. An isolated prolongation of the partial thromboplastin time in one patient was not given serious consideration because a liver biopsy done five months previously had been uneventful. Although one patient had bled after a previous liver biopsy, the second procedure was undertaken when all her coagulation studies were found to be normal. Another patient, who had bled following delivery of her last baby, did not report this history until after the biopsy was done. The patient with a platelet count of less than 50,000 per cu mm received platelet transfusions but she bled nonetheless. None of the control patients received fresh frozen plasma or platelets.

One pass with the biopsy needle was made in 20 of the 22 bleeding patients and 38 of the 41 control patients. Two passes were made in one bleeding patient and three control patients. Three passes were made in one patient who bled. Liver biopsies were done by both experienced (fellows, faculty and practicing physicians) and relatively inexperienced (medical residents) operators. Bleeding was not more frequent in inexperienced hands.

The indications for biopsy in the ten bleeding patients who had one or more contraindications to biopsy were alcoholic liver disease (two patients), chronic hepatitis (four patients), acute viral hepatitis (one patient), lymphoma staging (one patient) and unexplained hepatomegaly (two patients).

Review of the hepatic histology did not show any large hepatic arteries in the biopsy specimens from those who bled.

Discussion

Major bleeding followed percutaneous liver biopsy in one of every 140 patients (0.7 percent).

TABLE 3.—*Initial Indications of Bleeding**

	Bleeding (22)	*Control (41)*
Fall in mean arterial pressure	7	0
Rise in pulse rate	1	1
Simultaneous change in blood pressure and pulse	14	0
Right upper quadrant pain requiring narcotic analgesia	12	5

*Differences between bleeding and control groups with respect to fall in mean arterial pressure, simultaneous change in blood pressure and pulse and right upper quadrant pain are all significant at $P<0.001$.

TABLE 4.—*Relative Contraindications to Liver Biopsy*

	Bleeding (22)	*Control (41)*
Prothrombin time <50 percent*	4	0
PTT >10 seconds over control	1	1
Platelets <50,000 per cu mm	1	0
Past history of bleeding	1	0
Abnormal bleeding time	0	1
Prothrombin time <50 percent and PTT >10 seconds over control*	2	0
Past history of bleeding and PTT >10 seconds over control	1	0
TOTAL†	10	2

PTT—partial thromboplastin time

*The difference between the bleeding and control patients in the number with a prothrombin time <50 percent is significant at $P<0.003$.

†The difference between the bleeding and control patients in the number with one or more contraindications to biopsy is significant at $P<0.001$.

This rate is higher than the 0.08 percent to 0.2 percent reported previously in two large surveys.[2,6] We believe that these surveys may have underestimated the true incidence of this complication. Our figures are drawn from three closely allied hospitals where we kept records of most liver biopsies performed and noted any subsequent complications. Had we not done this, it is likely we would have been unaware of the five patients in whom transfusions were not needed, and may have missed some of those in whom transfusions were required. It would not be unreasonable to suspect that similar cases were missed in the previous reports. If so, most published rates may be artificially low and the true rate closer to ours. Two small series do report an incidence of hemorrhage approximating our (0.4 percent and 0.9 percent)[10,11] and Perrault and co-workers in a series of 1,000 patients report a rate of 0.5.[12]

Bleeding occurs sufficiently frequently to warrant concern and a search for possible causes. We use a 16-gauge needle which has an external diameter of 1.6 mm. This is larger than the 1.2-mm caliber of the standard Menghini needle and produces (in our opinion) a better specimen. Others have claimed, however, that the risk of the procedure increases geometrically with the diameter of the needle.[2,8,13] A diameter of 2 mm or more appears particularly dangerous and a diameter of 0.7 mm carries very little risk.[2,14] Whether the 1.6-mm needle is more dangerous than the 1.2-mm needle remains to be shown. The possibility exists, however, that we have incurred more bleeding as a price for obtaining a larger specimen.

We found that bleeding is more likely to occur in patients with definite histologic liver disease. This complements the findings of Perrault who noted that the overall complication rate for liver biopsy was higher in patients with cirrhosis or hepatitis than in those with other disorders.[12] Although our findings might suggest that bleeding is more common because there is a severe structural abnormality of the liver, we think it far more likely that the liver disease causes clotting and other abnormalities which in turn predispose the patient to bleeding.

This study has shown convincingly that relative contraindications to liver biopsy are present more frequently in patients who bleed than in those who do not. This is not to say that all patients with these contraindications will bleed following liver biopsy. To estimate the actual risk of these abnormalities would require liver biopsy in large numbers of patients with one or more contraindications to biopsy. As one small measure of the risk, liver biopsies were done at Stanford (during a six-year period) in 49 patients with a prothrombin time less that 50 percent or a thromboplastin time greater than 10 seconds over control. Three of these 49 patients bled (an incidence of 6.1 percent, a rate which is sixfold higher than the 0.9 percent rate in the remaining 633 patients). Whatever the true risk with these relative contraindications to biopsy, we believe that their presence in any given patient should give pause to those considering this procedure. In that light, it is difficult to see why the clinical diagnosis of alcoholic liver disease or acute viral hepatitis required a liver biopsy in three patients with a documented contraindication. If a liver biopsy is deemed absolutely necessary, it would be wise to correct any clotting abnormalities completely. This was not always done in our patients. We cannot guarantee that doing so would have prevented the bleeding episodes. However, liver biopsies have been carried out safely in patients with hemophilia when their factor deficiencies were fully corrected.[15]

We believe that some of the bleeding episodes in our patients could have been prevented with more careful attention to the indications and contraindications to biopsy, and more vigorous correction of recognized clotting abnormalities.

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